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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/817,044	04/02/2004	Young Hoon Park	A36218	3943

4372 7590 02/27/2008
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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
02/27/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/817,044	PARK ET AL.	
	Examiner	Art Unit	
	NINA A. ARCHIE	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9,13 and 23-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23* is/are allowed.

6)☒ Claim(s) *1-4,9,24 and 25* is/are rejected.

7)☒ Claim(s) *5 and 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is responsive to Applicant's amendment and response filed on 5/31/2007. Claims 6, 7 and 14-22 have been withdrawn. Claims 8 and 10-12 have been cancelled. Claims 1-5, 9, 13 and 23-24 are under examination.

Claim Objections/Rejections Withdrawn

2. In view of the Applicant's amendment and remark the following objections/rejections are withdrawn.

a) Objection to Claims 1-3, 5, 9 and 24 is withdrawn in light of light of applicant's amendment.

Claim Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moeckel et al US patent 6,107,063 issued August 22, 2000 in view of Eikmanns et al US patent 6,420,151 issued July 16, 2002, Palmeros et al 2000 Gene 247 255-264, and Debahov et al US patent 4,278,765 issued August 22, 2000 is maintained for the reason set forth in the previous office action.

Claim 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moeckel et al US patent 6,107,063 issued August 22, 2000 in view of Eikmanns et al US patent 6,420,151 issued July 16, 2002, Palmeros et al 2000 Gene 247 255-264, and Debahov et al US patent 4,278,765 issued August 22, 2000.

Applicant arguments:

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moeckel et al, US patent 6,107,063 (issued August 22, 2000), in view of Eikmanns et al, US patent 6,420,151 (issued July 16, 2002), Palmeros et al, 2000 Gene 247 255- 264, and Debahov et al, US patent 4,278,765 (issued August 22, 2000). The Examiner applies this same rejection to claim 24. Applicants respectfully but vigorously traverse this rejection. In order to sustain a prima facie case of obviousness, the cited art must motivate the cited combination and provide a likelihood of success in arriving at the invention through such combination. Although applicants understand that Moeckel and Eikmanns teach two different ways to mutate E. coli, applicants do not understand why one of skill in the art would have been motivated to combine such independent methods. In fact, one could argue that each of Moeckel and Eikmanns would have taught against such combination because their respective methods function successfully for their respective purposes. For instance, as the Examiner has explained, Eikmanns teaches a method to produce amino acids wherein the method eliminates unwanted side effects. Nothing in such disclosure suggests combining this method with yet another, different method, for any reason. Palermos and Debabov teach basic methods and research tools available at the time of the invention; they do not teach a problem that needs to be cured in either of Moeckel or Eikmanns' teachings, particularly a problem that would be cured by the combination of these two references. Thus, they do not provide any motivation to combine Moeckel and Eikmanns.

Additionally, it is not clear that one of skill in the art, in fact, would have had an expectation of arriving at the claimed invention based upon the cited references alone or in

combination. Moeckel discloses a method for producing L-isoleucine using a mutation in the region of the gene coding for the allosteric domains of threonine dehydrates. By the mutation, threonine dehydratase, which is inhibited by the feedback of the end product of the biosynthetic chain, L-isoleucine, is no longer inhibited by L- isoleucine feedback (See Figure 1, column 2, lines 7-15). Accordingly, threonine dehydrate functions as the degradation enzyme of L-threonine irrespectively of the amount of L-isoleucine. In contrast, according to the present invention, threonine degradation-associated operon (tdcBC operon) is inactivated such that threonine dehydratase cannot degrade L-threonine to ketobuyrate. The present invention functions because of the relationship between the production of L-threonine and the inactivation of the tdcBC operon and the inactivated pckA gene. Moeckle, which involves a completely different mechanism from that of the present invention, would not direct the skilled artisan toward applicants' invention or provide a likelihood of success according to such invention. Eikmanns, which discloses a nucleotide sequence encoding the pckA gene and a method for producing lysine or threonine using a pck gene-defective microorganism, likewise provides no suggestion that its teachings should be combined with an inactivated tdcBC operon. And to do so in view of Moeckle, would have been problematic. For instance, page 4, paragraph [0010] of the instant application, teaches that if the tdcBC operon is not inactivated, the production yield of L-threonine is a problem because the pathways for degradation and intracellular influx of synthesized L-threonine are still activated in the microorganism. The secondary references of Palermos and Debabov do not cure these problems. Finally, applicants point out that the E. coli of the present invention, which comprises an inactivated tdcBC operan and an inactivated pckA gene, produces a high concentration of L-threonine, even when the concentration of the glucose in the medium surrounding such E. coli is very high (see paragraph [0012]. Nothing in any of the cited references, alone or in combination, teach this feature of the claimed invention, which is recited explicitly in new claim 25.

Examiner's Response to Applicant's Arguments:

Examiner disagrees with Applicant's assertion as set forth supra. The claims are drawn to an isolated and purified *Escherichia coli* strain comprising an inactivated chromosomal tdcBC and inactivated pckA genes, wherein the chromosomal tdcBC operon and the chromosomal

pckA gene have been inactivated. Moeckel et al teaches an *E. coli* strain for the production of threonine and the *E. coli* strain is genetically engineered in that the threonine dehydratase gene (tdcBC operon) of a threonine-producing *Escherichia coli* strain is mutated to deregulate the feedback inhibition of L-isoleucine. Moeckel et al further teaches *E. coli* strain is inactivated by exchanging of one or several bases in the region coding for the allosteric domains of the enzyme and that at least one amino acid in the amino acid sequence of the allosteric domains is replaced by a different one. Moeckel et al further teach that threonine dehydratase is mutated in a host cell producing threonine. Eickmanns et al teaches a threonine producing *E. coli* strain that has an attenuated pckA gene. Eickmanns et al teach that the attenuation of the pck gene is advantageous, for the production of L-amino acids, in particular threonine. Eickmanns et al teach the mutant pck gene is introduced into a threonine producing *Escherichia coli* strain. Therefore, the DNA fragments coding for the mutant pck gene in *Escherichia coli* can be obtained by recombinant DNA by introducing amino acid replacement, insertion, or deletion into a pck gene as a wild type enzyme (see abstract, column 2 lines 1-40, columns 3-4, column 6 lines. 60-65, and Examples 1 and 7-8). Further more because both cited art teaching the production of L-threonine from an E.coli strain, the cited art does motivate the cited combination and provide a likelihood of success in arriving at the invention through such combination. Applicant states that the present invention functions because of the relationship between the production of L-threonine and the inactivation of the tdcBC operon and the inactivated pckA gene. The claims are products by process claims and the patentability of a product does not depend on its method of production (see MPEP 2113). Therefore the claims are drawn to the isolated and purified *Escherichia coli* strain comprising an inactivated chromosomal tdcBC and inactivated pckA genes and an isolated or purified L-threonine producing strain of *Escherichia coli* strain, wherein the chromosomal tdcBC operon and the chromosomal pckA gene have been inactivated that produces L-threonine which meets the limitations of the claims.

As to the secondary references, Palmeros et al teaches general teachings of inserting a cassette with the DNA fragment into a cleavage site. Palmeros et al teaches a DNA fragment with loxp sites and antibiotic resistance gene having site-specific recombinase such as Cre is inserted into the genome of the *Escherichia coli* strain to allow homologous recombination between the DNA gene fragment and the gene on the chromosome to elute recombinant strains

having the deactivated mutant gene. Debabov et al teach a method for constructing strains that possess an increased capability of producing the required amino acid (i.e. threonine), which produce amino acids by genetic engineering techniques (see Examples). Therefore one would be motivated at the time the invention was to introduce a DNA fragment (i.e. pck A gene) into the genome of the *Escherichia coli* strain to allow homologous recombination because Palmeros et al teaches that the system of inserting a DNA fragment into the genome of the *Escherichia coli* strain to allow homologous recombination is useful because no antibiotic resistance markers stay behind on the *Escherichia coli* chromosome and therefore the cell does not carry an antibiotic resistance gene that subsequently would prevent the selection for plasmids or other chromosomal modifications that would depend on such markers and Debabov et al teach having a recipient strain having the mutation blocking the synthesis of the selected amino acid (i.e. threonine) in this strain and the mutation partly blocking the related step of metabolism of the selected amino acid (i.e. threonine) can yield the strain capable of increased productivity of the selected amino acid (i.e. threonine) which therefore meets the limitations of the claims.

The rejection is based on claims 1-4 and 24 therefore the newly cited claim (claim 25) is not considered in the rejection discussed as set forth supra.

Furthermore given that a tdcBC mutation and a pckA mutation have both separately been used to increase production of L-amino acids, it remains obvious to combine them, even without an express statement of motivation. KSR forcloses the argument that a specific teaching, suggestion, or motivation is required to support a finding a obviousness. See the recent Board Decision Ex parte Smith, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007 (citing KSR, 82 USPQ2d at 1396) available at (http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf).

As outlined previously, the instant claims (claims 1-4) are to drawn to an isolated and purified *Escherichia coli* strain comprising an inactivated chromosomal tdcBC and inactivated pckA genes. At the outset it is noted that Applicants' specification acknowledges that the threonine dehydratase operon and tdcBC operon are the same as described in the literature (see page 4, paragraph [0009]).

Moeckel et al teaches an *E. coli* strain for the production of threonine. The *E. coli* strain is genetically engineered in that the threonine dehydratase gene (tdcBC operon) of a threonine-producing *Escherichia coli* strain is mutated to deregulate the feedback inhibition of L-isoleucine (see abstract, column 1 lines 5-15). Moeckel et al teach that threonine dehydratase (tdcBC operon) is inactivated by exchanging of one or several bases in the region coding for the allosteric domains of the enzyme and that at least one amino acid in the amino acid sequence of the allosteric domains is replaced by a different one. Moeckel et al teach that threonine dehydratase is mutated in a host cell producing threonine (see column 2 lines).

Moeckel et al does not teach an isolated and purified *Escherichia coli* strain inactivated pckA gene, wherein the pckA gene is inactivated by introducing a foreign pckA gene fragment containing an antibiotic resistance gent having a site-specific recombinase binding site at each of both ends thereof into a parent *Escherichia coli* strain containing an L-threonine degradation-associated operon, tdcBC, that is inactivated, and then allowing homologous recombination between the foreign pckA gene fragment and the pckA gene on chromosome to inactivate the chromosomal pckA gene, wherein the pckA gene is inactivated by removal of the antibiotic resistance gene incorporated there into by the activity of the site-specific recombinase expressed in the Escherichia coli strain and the presence of one copy of the binding site of the site-specific recombinase in the chromosomal pckA gene, wherein the site-specific recombinase is FLP, Cre or XerC/D.

Eickmanns et al US patent 6,420,151 teaches a threonine producing *E. coli* strain that has an attenuated pckA gene. Eickmanns et al teach that the attenuation of the pck gene is advantageous, for the production of L-amino acids, in particular threonine, to eliminate undesirable side reactions. Eickmanns et al teach the mutant pck gene is introduced into a threonine producing *Escherichia coli* strain. Therefore, the DNA fragments coding for the mutant pck gene in *Escherichia coli* can be obtained by recombinant DNA by introducing amino acid replacement, insertion, or deletion into a pck gene as a wild type enzyme (see abstract, column 2 lines 1-40, columns 3-4, column 6 lines. 60-65, and Examples 1 and 7-8).

Palmeros et al teaches generally inserting a cassette with the DNA fragment into a cleavage site. Palmeros et al teaches a DNA fragment with loxp sites and antibiotic resistance

gene having site-specific recombinase such as Cre is inserted into the genome of the *Escherichia coli* strain to allow homologous recombination between the DNA gene fragment and the gene on the chromosome to clute recombinant strains having the deactivated mutant gene (see "Material and Methods").

Debabov et al teach a method for constructing strains that possess an increased capability of producing the required amino acid (i.e. threonine), which produce amino acids by genetic engineering techniques (see Examples).

It would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to inactivate the chromosomal tdcBC operon of the *E. coli* strain (threonine dehydratase gene) as taught by Moeckel et al and to inactivate the pckA gene of the E. coli strain as taught by Eickmanns et al because both teach E. coli strains to produce L-threonine. It would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to introduce a DNA fragment (i.e. pck A gene) into the genome of the *Escherichia coli* strain to allow homologous recombination because Palmeros et al teaches that the system of inserting a DNA fragment into the genome of the *Escherichia coli* strain to allow homologous recombination is useful because no antibiotic resistance markers stay behind on the *Escherichia coli* chromosome and therefore the cell does not carry an antibiotic resistance gene that subsequently would prevent the selection for plasmids or other chromosomal modifications that would depend on such markers and Debabov et al teach having a recipient strain having the mutation blocking the synthesis of the selected amino acid (i.e. threonine) in this strain and the mutation partly blocking the related step of metabolism of the selected amino acid (i.e. threonine) can yield the strain capable of increased productivity of the selected amino acid (i.e. threonine).

As outlined previously, the instant claim (claim 24) are to drawn to an isolated or purified L-threonine producing strain of *Escherichia coli* wherein the chromosomal tdcBC operon and the chromosomal pckA gene have been inactivated. At the outset it is noted that Applicants' specification acknowledges that the threonine dehydratase operon and tdcBC operon are the same as described in the literature (see page 4, paragraph [0009]).

Moeckel et al teaches an *E. coli* strain for the production of threonine. The *E. coli* strain is genetically engineered in that the threonine dehydratase gene (tdcBC operon) of a threonine-producing *Escherichia coli* strain is mutated to deregulate the feedback inhibition of L-isoleucine (see abstract, column 1 lines 5-15). Moeckel et al teach that threonine dehydratase (tdcBC operon) is inactivated by exchanging of one or several bases in the region coding for the allosteric domains of the enzyme and that at least one amino acid in the amino acid sequence of the allosteric domains is replaced by a different one. Moeckel et al teach that threonine dehydratase is mutated in a host cell producing threonine (see column 2 lines).

Eickmanns et al US patent 6,420,151 teaches a threonine producing *E. coli* strain that has an attenuated pckA gene. Eickmanns et al teach that the attenuation of the pck gene is advantageous, for the production of L-amino acids, in particular threonine, to eliminate undesirable side reactions. Eickmanns et al teach the mutant pck gene is introduced into a threonine producing *Escherichia coli* strain. Therefore, the DNA fragments coding for the mutant pck gene in *Escherichia coli* can be obtained by recombinant DNA by introducing amino acid replacement, insertion, or deletion into a pck gene as a wild type enzyme (see abstract, column 2 lines 1-40, columns 3-4, column 6 lines. 60-65, and Examples 1 and 7-8).

Palmeros et al teaches generally inserting a cassette with the DNA fragment into a cleavage site. Palmeros et al teaches a DNA fragment with loxp sites and antibiotic resistance gene having site-specific recombinase such as Cre is inserted into the genome of the *Escherichia coli* strain to allow homologous recombination between the DNA gene fragment and the gene on the chromosome to elute recombinant strains having the deactivated mutant gene (see "Material and Methods").

Debabov et al teach a method for constructing strains that possess an increased capability of producing the required amino acid (i.e. threonine), which produce amino acids by genetic engineering techniques (see Examples).

It would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to inactivate the chromosomal tdcBC operon of the *E. coli* strain (threonine dehydratase gene) as taught by Moeckel et al and to inactivate the chromosomal pckA gene of the E. coli strain as taught by Eickmanns et al because both teach E. coli strains to produce L-threonine. It would have been prima facie obvious to one having ordinary skill in the

art at the time that the invention was made to introduce a DNA fragment (i.e. pck A gene) into the genome of the *Escherichia coli* strain to allow homologous recombination because Palmeros et al teaches that the system of inserting a DNA fragment into the genome of the *Escherichia coli* strain to allow homologous recombination is useful because no antibiotic resistance markers stay behind on the *Escherichia coli* chromosome and therefore the cell does not carry an antibiotic resistance gene that subsequently would prevent the selection for plasmids or other chromosomal modifications that would depend on such markers and Debabov et al teach having a recipient strain having the mutation blocking the synthesis of the selected amino acid (i.e. threonine) in this strain and the mutation partly blocking the related step of metabolism of the selected amino acid (i.e. threonine) can yield the strain capable of increased productivity of the selected amino acid (i.e. threonine).

New Grounds of Rejection

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 9 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statuatory subject matter.

The claimed invention is drawn to a product of nature. Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, purity of naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui 156 USPQ 426 (1966). However when purity results in new utility, patentability is considered. Merck co. V. Chase Chemical Co. 273 F. Supp 68 (1967). See also American Wood v. Fiber Disintegrating Co., 90 US 566 (1974);American Fruit Growers v. Brogdex Co. 283 US 1 (1931); Funk Brothers Seed Co. V. Kalo Innoculant Co. 33 US 127 (1948). In the instant case recitation

of an inactivated gene does not indicate the hand of man because naturally occurring mutations can inactivate genes as such, the claimed *Escherichia coli* strains are deemed products of nature.

Claim Rejections - 35 USC § 112

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. As to claim 9, a independent claim, recites the limitation "the E.coli strain. There is insufficient antecedent basis for these limitations in the claims.

As to claim 25 a dependent claim, recites the phrase "high" and "very high". However, neither the claim nor the specification clearly defines nor sets forth the meaning or means to assess "high" and "very high". "High" and "very high" has no art defined meaning with respect to a genes. Therefore, the skilled artisan would not be readily apprised of the metes and bounds of "high" and "very high" nor how to assess such. It is unclear how to interpret what degree of similarity is required to correspond to something and inasmuch as it is not a recognized term and not defined in the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claim 1, 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moeckel et al US patent 6,107,063 issued August 22, 2000 in view of Eikmanns et al US patent 6,420,151 issued July 16, 2002.

The claims are drawn to an isolated and purified *Escherichia coli* strain comprising an inactivated chromosomal tdcBC and inactivated pckA genes, wherein such strain produces a high concentration of L-threonine when the concentration of the glucose in the medium surrounding such strain is very high (claim 1); an isolated or purified L-threonine producing strain of *Escherichia coli* wherein the chromosomal tdcBC operon and the chromosomal pckA gene have been inactivated, wherein such strain produces a high concentration of L-threonine when the concentration of the glucose in the medium surrounding such strain is very high (claim 24). At the outset it is noted that Applicants' specification acknowledges that the threonine dehydratase operon and tdcBC operon are the same as described in the literature (see page 4, paragraph [0009]).

Moeckel et al teaches an *E. coli* strain for the production of threonine. The *E. coli* strain is genetically engineered in that the threonine dehydratase gene (tdcBC operon) of a threonine-producing *Escherichia coli* strain is mutated to deregulate the feedback inhibition of L-isoleucine (see abstract, column 1 lines 5-15). Moeckel et al teach that threonine dehydratase (tdcBC operon) is inactivated by exchanging of one or several bases in the region coding for the allosteric domains of the enzyme and that at least one amino acid in the amino acid sequence of

the allosteric domains is replaced by a different one. Moeckel et al teach that threonine dehydratase is mutated in a host cell producing threonine (see column 2 lines). Moeckel et al teach *E. coli* strains are cultured Luria-Bertani medium to produce L-threonine (see Example 1.1).

Eickmanns et al US patent 6,420,151 teaches a threonine producing *E. coli* strain that has an attenuated pckA gene. Eickmanns et al teach that the attenuation of the pck gene is advantageous, for the production of L-amino acids, in particular threonine, to eliminate undesirable side reactions. Eickmanns et al teach the mutant pck gene is introduced into a threonine producing *Escherichia coli* strain. Therefore, the DNA fragments coding for the mutant pck gene in *Escherichia coli* can be obtained by recombinant DNA by introducing amino acid replacement, insertion, or deletion into a pck gene as a wild type enzyme (see abstract, column 2 lines 1-40, columns 3-4, column 6 lines. 60-65, and Examples 1 and 7-8). Eickmanns et al teach an *E. coli* strain that produces a concentration of L-threonine were cultured in Luria-Bertani complex medium plus 1% glucose (see Example 8 and Table 5). Eichmanns et al teaches the culture medium to be used must meet the requirements of the particular strains in a suitable manner and that descriptions of culture media for various microorganisms are contained in the handbook "Manual of Methods for General Bacteriology" of the American Society for Bacteriology (Washington D.C., USA, 1981) Sugars and carbohydrates, such as e.g. glucose (see column 7 see lines 31-40).

Examiner interprets "high concentration" as any concentration since there is no defined meaning of high concentration in the specification.

It would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to inactivate the chromosomal tdcBC operon of the *E. coli* strain (threonine dehydratase gene) as taught by Moeckel et al and to inactivate the chromosomal pckA gene of the E. coli strain as taught by Eickmanns et al because both teach E. coli strains to produce L-threonine. It would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to produce a high concentration of L-threonine when the concentration of the glucose is in the medium surrounding the strain is high because Eichmanns et al teach an *E. coli* strain cultured in Luria-Bertani complex medium with glucose and furthermore both Moeckel et al and Eichmanns et al teach Luria-Bertani medium.

Citation of Relevant Art

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ozaki et al. Agric. Biol. Chem. 47 No. 7 (1983) 1569-1576 teaches factors that cause an increase in lysine production using various mutants.

Status of the Claims

8. No claims are allowed.

Claims 1-4, 9, 24, and 25 are rejected.

Claims 5 and 13 are objected as being dependent from a rejected claim.

Claim 23 is free of the art.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from

a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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